A Novel Non-phosgene Process for the Synthesis of Methyl N-Phenyl Carbamate from Methanol and Phenylurea: Effect of Solvent and Catalyst

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A novel environmentally benign process for the synthesis of methyl N-phenyl carbamate (MPC) from methanol and phenylurea was studied. Effect of solvent and catalyst on the reaction behavior was investigated. The IR spectra of methanol and phenylurea dissolved in different solvents were also recorded. Compared with use of methanol as both a reactant and a solvent, phenylurea conversion and selectivity to MPC increased by using toluene, benzene or anisole as a solvent, while phenylurea conversion decreased slightly by using n-octane as a solvent. The phenylurea conversion declined nearly 50% when dimethyl sulfoxide (DMSO) was used as a reaction media, and MPC selectivity decreased as well. The catalytic reaction tests showed that a basic catalyst enhanced the selectivity to MPC while an acidic catalyst promoted the formation of methyl carbamate and aniline. Moderate degree of basicity showed the best catalytic performance in the cases studied.

Keywords methyl N-phenyl carbamate synthesis, phenylurea, phosgene-free, solvent effect, acid-base catalyst

Introduction

Isocyanate compound as an important raw material in organic and polymer chemistry has been produced commercially by a reaction between amine and phosgene, in which toxic reagent of phosgene was used and a stoichiometric amount of hydrogen chloride was co-produced as a by-product that causes serious corrosion. Replacement of this process by an environmentally benign phosgene-free process is of great significance. Methyl N-phenyl carbamate (MPC) is an important precursor for preparing isocyanates since it produces isocyanates and alcohols in good yields by thermal decomposition. Several methods for preparing N-phenyl carbamates without using phosgene have been reported, including reductive carbonylation of nitro aromatics, oxidative carbonylation of amines, methoxy carbonylation of aniline with dimethyl carbonate (DMC), and alcoholysis of diphenylurea. Some of these methods, however, have some limitations. For example, the carbonylation reaction should be carried out under high pressures in the presence of noble metal such as Pt, Pd, Ru and Rh catalysts; the methoxy carbonylation of aniline gives high selectivity to MPC under mild conditions in the presence of Pb-based catalysts, which seems promising, but it involves a difficult process of separation of methanol from DMC azotrope, and DMC is relatively expensive. The synthesis of MPC by alcoholysis of diphenylurea will be accompanied by the formation of equimolar amount of aniline. The separation of MPC from aniline is quite difficult due to their very close boiling points. Phenylurea as an asymmetric urea that can be prepared in good yield by a non-catalytic reaction between urea and aniline hydrochloride is a compound inexpensive and readily available for the synthesis of MPC compared with dialkyl carbamates. But the relevant study has not been found in the literature. Here we report the effect of solvent and catalyst on the reaction between phenylurea and methanol for the synthesis of MPC.

Experimental

The reaction between methanol and phenylurea was carried out in a 100 mL autoclave. In a typical experiment, 6.81 g (0.05 mol) of phenylurea (C.P., Beijing Chemical Plant), 12.02 g (0.375 mol) of methanol (A.R., Shanghai Zhenxing Chemical Plant), 0.3 g of catalyst and 40 mL of solvent (A.R.) were charged into the reactor. The catalyst used was commercially available reagent with A.R. purity as-obtained without further treatment unless otherwise noted. The reactor was
purged 5 times with argon at 0.6 MPa, and then heated at the rate of 7 K/min to 433 K under vigorous stirring. After reaction at 433 K for 4.5 h, the reactor was cooled quickly to 333 K and depressurized. A certain amount of biphenyl as an internal standard was added into the reaction mixture. The reaction mixture was analyzed by using GC-MS for qualification and by a temperature programmable gas chromatograph equipped with a flame ionization detector and an OV-1701 capillary column (50 m × 0.32 mm) for quantification.

FTIR absorption spectra of the samples were measured by KBr disc method at room temperature on a Bruker Vector 22 FTIR spectrometer over the range of 4000–400 cm⁻¹. The phenylurea sample was prepared by mixing phenylurea with dry KBr fine powders and pressing the resultant mixture into a disc. The liquid samples were prepared by dropping the liquid onto a pretreated KBr disc to form a thin film.

Results and discussion

Effect of solvent

From the GC-MS data, it is found that methyl carbamate (MC), methyl N-phenyl carbamate (MPC), phenyl isocyanate (PIC) and aniline are all products detected in solvent in all cases studied. Based on the reaction products it is deduced that the reactions taking place in the system may include the followings:

\[
\begin{align*}
\text{HNCH}_2 \text{CH}_3 + \text{CH}_3\text{OH} & \rightarrow \text{HNO} \text{CCH}_3 + \text{NH}_3 \quad (1) \\
\text{HNCH}_2 \text{COCH}_3 + \text{CH}_3 \text{OH} & \rightarrow \text{NH}_2 \text{COCH}_3 + \text{C}_6\text{H}_5 \text{NH} \quad (2) \\
\text{HNO} \text{CCH}_3 & \rightarrow \text{C}_6\text{H}_5 \text{NO} + \text{CH}_3\text{OH} \quad (3)
\end{align*}
\]

The reaction results of methanol with phenylurea in different solvents in the absence of catalyst are listed in Table 1. The phenylurea conversion was 73.7% with MPC being the main product when methanol was used as both a reactant and a solvent. Meanwhile, MPC decomposition product of phenyl isocyanate (PIC) was also formed. When toluene, benzene or anisole was used as a solvent, the phenylurea conversion and MPC selectivity decreased markedly when the reaction mixture was carried out in dimethyl sulfoxide (DMSO). The phenylurea conversion decreased slightly when n-octane was used as a solvent. Moreover, for the reactions performed in a solvent other than methanol the selectivity to decomposition product of phenyl isocyanate was higher than that in methanol solvent.

In order to get an insight into the mechanism of reaction and of the solvent effect, FT-IR spectra of methanol, phenylurea, and phenylurea dissolved in methanol and in different solvents such as anisole, toluene, DMSO were recorded. Figure 1a shows the FT-IR spectra of methanol, phenylurea and phenylurea dissolved in methanol. In the FT-IR spectra of methanol a broad absorption band in 3100–3600 cm⁻¹ region which was assigned to the associated O—H stretching vibrations, absorption bands at 2833 and 2946 cm⁻¹ ascribable to C—H stretching mode as well as a band at 1031 cm⁻¹ attributable to C—O stretching mode appeared. When phenylurea and methanol were dissolved in toluene or anisole, the broad band of the band was broadened. Meanwhile, absorptions of NH₂, NH, N—C=O modes were also shifted to lower wavenumbers, which means that there exist hydrogen bond and dipole-dipole interactions between methanol and phenylurea molecules. When phenylurea and methanol were dissolved into different solvents such as toluene, anisole and DMSO, the FT-IR spectra (Figure 1b) changed noticeably. When phenylurea was dissolved in methanol, the absorption of C=O stretching mode was shifted to 1670 cm⁻¹, and half-width of the band was broadened. Meanwhile, absorptions of NH₂, NH, N—C=O modes were also shifted to lower wavenumbers, which means that there exist hydrogen bond and dipole-dipole interactions between methanol and phenylurea molecules. When phenylurea and methanol were dissolved into different solvents such as toluene, anisole and DMSO, the FT-IR spectra (Figure 1b) changed noticeably. When phenylurea was dissolved in methanol, the absorption of C=O stretching mode was shifted to 1670 cm⁻¹, and half-width of the band was broadened. Meanwhile, absorptions of NH₂, NH, N—C=O modes were also shifted to lower wavenumbers, which means that there exist hydrogen bond and dipole-dipole interactions between methanol and phenylurea molecules. When phenylurea and methanol were dissolved into different solvents such as toluene, anisole and DMSO, the FT-IR spectra (Figure 1b) changed noticeably. When phenylurea was dissolved in methanol, the absorption of C=O stretching mode was shifted to 1670 cm⁻¹, and half-width of the band was broadened. Meanwhile, absorptions of NH₂, NH, N—C=O modes were also shifted to lower wavenumbers, which means that there exist hydrogen bond and dipole-dipole interactions between methanol and phenylurea molecules.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Phenylurea conv. %</th>
<th>MPC</th>
<th>Aniline</th>
<th>PIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methanol</td>
<td>73.7</td>
<td>65.1</td>
<td>34.3</td>
<td>0.6</td>
</tr>
<tr>
<td>DMSO</td>
<td>43.2</td>
<td>49.6</td>
<td>47.7</td>
<td>2.7</td>
</tr>
<tr>
<td>Benzene</td>
<td>83.7</td>
<td>76.1</td>
<td>21.8</td>
<td>2.1</td>
</tr>
<tr>
<td>Toluene</td>
<td>85.0</td>
<td>79.7</td>
<td>16.1</td>
<td>4.2</td>
</tr>
<tr>
<td>Anisole</td>
<td>78.1</td>
<td>66.4</td>
<td>31.1</td>
<td>2.5</td>
</tr>
<tr>
<td>n-Octane</td>
<td>70.2</td>
<td>72.2</td>
<td>25.2</td>
<td>2.6</td>
</tr>
</tbody>
</table>

* Reaction conditions: T=160 °C, reaction time: 4.5 h, except using methanol as solvent, the molar ratio of methanol to phenylurea is 7.5.  
* MPC: methyl N-phenyl carbamate; PIC: phenyl isocyanate.
bers of NH₂, NH, N—C=O absorption were changed remarkably, indicating the strong interaction between the carbonyl group and the solvent. The broad band in 3100—3600 cm⁻¹ still appeared, indicating existence of OH association in DMSO.

In order to get an in-depth understanding of the direction of proton transfer during the reaction, the charge of each atom in phenylurea molecule was studied by quantum chemical calculation using density functional theory/Hartree-Fock hybrid method B3LYP. It was found from calculation that the natural bond orbital charge of nitrogen in —NH₂ is —0.8402 and in PhNH— —0.6504. Therefore, the proton is preferably transferred to —NH₂ to form —NH₃⁺ which is a weaker base and a better leaving group compared to the PhNH— group. After losing NH₃, MPC is formed as the product. When the reaction was carried out in different solvents, due to the different solvation of methanol and phenylurea, their reactivities are different. When protic methanol was used as both a solvent and a reactant, the nucleophilic reactivity of methanol was reduced by the intermolecular hydrogen bond. When the reaction was carried out in toluene, benzene or anisole, the intermolecular hydrogen bond was absent as observed in IR spectra, and the interaction between methanol and the solvent was a weak electron pair donor/acceptor (EPD/EPD) one which makes methanol a more active nucleophile. Meanwhile, the electrophilic reactivity of carbonyl carbon was not influenced by the solvation of toluene, benzene or anisole. Consequently, an increase in phenylurea conversion was observed. When

![Figure 2 Proposed reaction scheme of methanol with phenylurea.](image-url)
the reaction was performed in a strongly polar solvent like DMSO, strong interactions between carboxyl group of phenylurea and solvent as observed in FT-IR spectra inhibited the interaction of phenylurea with methanol. Meanwhile, the association of methanol still existed as observed in FT-IR, which reduced its nucleophilicity, and the phenylurea conversion was decreased consequently. The declined selectivity to MPC in DMSO solvent may be related to the weak acidity (or protic character) of DMSO which may interact with $\text{-NH}_2$ and decrease the electron density of $\text{-NH}_2$ and resultantly reduce the transferring possibility of proton to $\text{-NH}_2$. As for the non-polar n-octane, due to the poor miscibility of methanol with n-octane and relatively good solubility of phenylurea in octane, the interaction between solvent and solute was very weak. When n-octane was used as a reaction media, the phenylurea was partially dissolved in methanol and partially in n-octane. During reaction, methanol in n-octane might form small micelles under vigorous stirring, so the reaction was taking place within methanol droplets or at inter-phase between methanol and n-octane. Due to the concentration of phenylurea contacting with methanol decreased, the phenylurea conversion was decreased naturally.

Effect of catalyst

Table 2 lists the reaction results of methanol with phenylurea in the presence of a catalyst using toluene as a solvent. MPC selectivity was increased by using basic compound such as MgO, ZnO or ZrO$_2$ as a catalyst. Whereas the MPC selectivity was decreased by using acidic compound such as ZnCl$_2$ or Pb(NO$_3$)$_2$ as a catalyst. As discussed above, the product selectivity depends upon the leaving tendency of $\text{-NH}_2$ and $\text{PhNH}^-$ that is determined by their basicity and influence by the direction of proton transfer in the formed tetrahedral intermediate. In the cases of non-catalytic reactions, proton is preferably transferred to $\text{-NH}_2$ to form $\text{PhNH}^-$, and aniline and methyl carbamate are formed. As a result, the MPC selectivity is decreased. In the presence of an acidic catalyst, such as ZnCl$_2$ or Pb(NO$_3$)$_2$, the catalyst may preferentially interact with the terminal $\text{-NH}_2$ that has the highest electron density in phenylurea molecule to form a kind of complex. As a result, the electron density of $\text{-NH}_2$ is decreased after interaction with the catalyst and hence the driving force for the proton transfer to $\text{-NH}_2$ is decreased. If the proton is transferred to $\text{PhNH}^-$, it becomes a better leaving group, and aniline and methyl carbamate are formed. As a result, MPC selectivity is decreased. In the presence of a base catalyst such as MgO or ZnO, the catalyst may preferentially activate the methanol that is an acidic compound, increase its nucleophilicity and facilitate the proton transfer to $\text{-NH}_2$. As a consequence, MPC selectivity is increased. ZrO$_2$ is frequently classified into the amphoteric oxide, but some researchers in heterogeneous catalysis consider it as weakly basic oxide based on the adsorption behavior of acid compound. It is reported that zirconia strongly adsorbs the benzoate anion and is therefore classified into the weakly basic material.

Another important information in Table 2 is that the phenylurea conversion and MPC selectivity using strongly basic catalyst like KOH and NaOCH$_3$ are not as high as those using a weak base like Na$_2$CO$_3$ or TiO$_2$, which means that moderate degree of base is favorable to the reaction. The possible reason might be that the strong base may react with acidic methanol to form $\text{CH}_3\text{O}^-$ which has the higher electron density and nucleophilicity but is geometrically not favorable for the proton transfer, and hence the phenylurea conversion and MPC selectivity are not as high as those for moderate-strength base. The further research is under going to correlate the strength of basicity of a catalyst with its reaction behavior and to a detailed functioning mechanism.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Phenylurea Conv./%</th>
<th>MPC Selectivity/mol%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-catalytic</td>
<td>85.1</td>
<td>64.4</td>
</tr>
<tr>
<td>CuCl$_2$·2H$_2$O</td>
<td>84.6</td>
<td>51.7</td>
</tr>
<tr>
<td>ZnCl$_2$</td>
<td>76.5</td>
<td>41.6</td>
</tr>
<tr>
<td>Pb(NO$_3$)$_2$</td>
<td>84.5</td>
<td>58.3</td>
</tr>
<tr>
<td>MgO</td>
<td>86.3</td>
<td>73.3</td>
</tr>
<tr>
<td>ZrO$_2$</td>
<td>80.1</td>
<td>80.4</td>
</tr>
<tr>
<td>Cu$_2$O</td>
<td>74.0</td>
<td>61.1</td>
</tr>
<tr>
<td>ZnO</td>
<td>88.6</td>
<td>71.4</td>
</tr>
<tr>
<td>TiO$_2$ (anatase)</td>
<td>71.2</td>
<td>78.8</td>
</tr>
<tr>
<td>NaOCH$_3$</td>
<td>77.1</td>
<td>71.7</td>
</tr>
<tr>
<td>Na$_2$CO$_3$ (anhydrous)</td>
<td>81.1</td>
<td>79.9</td>
</tr>
<tr>
<td>KOH</td>
<td>83.5</td>
<td>68.6</td>
</tr>
</tbody>
</table>

Toluene was used as a solvent, molar ratio of methanol to phenylurea: 5. reaction temperature: 160 °C, amount of the catalyst charged: 0.3 g.

Summaries

A novel phosgene-free process for the synthesis of methyl N-phenyl carbamate (MPC) from methanol and phenylurea was studied. It was found that when toluene, benzene or anisole was used as a solvent, its solvation reduced the intermolecular associative hydrogen bond of methanol and made it more active as a nucleophile but had little influence on carbonyl carbon, hence the phenylurea conversion increased. When reaction took place in DMSO, the strong interactions between solvent and reactants reduced electrophilicity reactivity of carbonyl carbon and the nucleophilicity of methanol, as a result, a remarkable decrease in phenylurea conversion was observed. The catalytic reaction results indicated...
that a basic catalyst greatly enhanced the yield of MPC, whereas an acidic catalyst promoted the formation of aniline and methyl carbamate. In terms of MPC yield, moderate strength of basicity showed the best catalytic performance in the cases studied.

References

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